YANKEE DOODLING Douglas Kamerow

Paying for promising but unproven technologies

Is the policy on “coverage with evidence development” a helpful way forward?

Promising new medical technologies, especially expensive ones, pose a difficult problem for healthcare systems. If there is not enough evidence for conventional systematic reviews and technology assessments to find benefit, the default decision is that a new technology, whether drug, device, or surgical procedure, is not “covered” and thus not paid for. This seems reasonable when we are talking about a screening test or other preventive manoeuvre, since most would agree that we should require a high level of proof before exposing a well population to expensive and potentially harmful interventions. But what about when the person is sick, perhaps with advanced cancer, and the promising technology is a potentially lifesaving chemotherapeutic agent, a new surgical procedure, or a drug already approved but for a different condition?

On the other hand, to allow payment for such technologies might break the bank if the new interventions are expensive, and of course they may not work at all. Everyone's favourite cautionary example is high-dose chemotherapy with autologous bone marrow transplantation for advanced breast cancer. Hugely expensive but thought to be helpful, it was the subject of intense scrutiny and publicity in the US about 10 years ago. Many women with advanced breast cancer demanded that their health insurance plans cover the procedure and sued the companies in court when they did not. Only when a definitive randomised controlled trial found no benefit did the furore subside.

It seems that a middle ground between “yes” and “no” is needed in situations in which new technologies have suggestive but not definitive evidence of benefit, especially when they are thought to be breakthroughs or highly cost-effective treatments. Such a coverage option was first developed in the US in 1995 in response to another then-promising technology, lung volume reduction surgery (LVRS) for chronic obstructive lung disease. US government staff in the Medicare

programme, which pays for care for elderly people and some disabled patients, noticed a dramatic increase in insurance payments for this expensive and dangerous surgery in the early and mid-1990s. Surgical centres had developed a new, safer technique for the operation and were claiming great success in patients with end-stage lung disease, allowing them to walk and live normal lives again after surgery. A government-sponsored technology assessment, however, could find no supportive randomised evidence for the procedure, leading to a national non-coverage decision. This unleashed a political firestorm.

In 1995 Medicare announced an innovative response to this situation: it would cover LVRS, but only if patients consented to be randomised into a multi-centre trial sponsored by the National Institutes for Health comparing the surgery with optimal medical treatment. Medicare called this policy “coverage with evidence development.” The LVRS study was a challenging trial to perform, with much public controversy played out in the news media and even in Congress, but ultimately some 1200 patients were randomised. When the results were published, LVRS showed no overall survival advantage to intensive medical treatment, but selective improvements were seen in exercise capacity and quality of life for certain patients. The trial also highlighted the true risks of the surgery, as perioperative mortality was almost 10%. Although Medicare ultimately covered LVRS in selected patients, the trial results scared most referring doctors and patients away from it and it has been largely an abandoned procedure in the past five years.

But is it ethical to demand that patients who want a procedure be forced to enrol in a trial in which they are equally as likely to receive a control intervention as the treatment they are seeking? Lawyers, often representing the technology developers or “denied” patients, have argued that coverage with evidence development policies are

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coercive, unfair, and illegal. Ethicists disagree (*JAMA* 2006;296:988-90), as long as the technologies are chosen carefully and appropriately and the policies provide a net increase in coverage for technologies that would otherwise be denied approval.

Medicare staff have subsequently refined and reissued their policy on coverage with evidence development and more carefully justified its legal basis. It has been used to provide limited coverage for carotid artery angioplasty with stenting and for PET (positron emission tomography) scanning in the evaluation of dementia patients, both in the context of clinical trials. Most recently, the policy was used to mandate that expanded coverage of implantable cardioverter-defibrillators for prevention of sudden death be linked with patient enrolment in an ongoing national data register, which will allow assessment of who benefits from this technology and who does not.

The US experience with this issue was not lost on the UK Department of Health when it set up the National Institute for Health and Clinical Excellence (NICE) in 1999. It provided for a NICE recommendation category termed “approval only in the context of research” or OIR, which has been used sparingly since NICE was initiated. Kalipso Chalkidou and colleagues have recently reviewed the NICE experience with OIR recommendations (*Journal of the Royal Society of Medicine* 2007;100:453-60). They conclude that OIR, when used sparingly, has provided an important alternative to a “yes” or “no” decision on the appropriateness of technologies. But they concede that they face twin challenges similar to their US (and indeed, worldwide) colleagues: developing a clear and reproducible set of criteria for when to use coverage with evidence development, and ensuring the timeliness and funding of the research studies they recommend.

Douglas Kamerow is former US assistant surgeon general and associate editor, *BMJ*
dkamerow@bmj.com